REMARKS

In the Office Action dated November 7, 2002, claims 1, 3, 5-11, 13-15 and 17-23 in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks.

Claims 1, 3, 5-11, 13-15, 17-22 and 23 were rejected under 35 USC §112, first paragraph, as lacking enablement. Though applicants respectfully disagree, in order to further the prosecution of the present application, claims 1, 3, 5-11 and 13-23 have been canceled and new claims added to the application. The new claims indicate that the Helicobacter immunogen consists of urease A and urease B or immunologically reactive fragments of urease A and urease B. Applicants point out that in the previously submitted declaration the expression of ureaseA and urease B was regulated within the plasmid pYZ97 by joint promotors. That is the "cryptic" promotor (cf.US 2002/0161192 of CIP, paragraph 0065, paragraph 0066, SEQ ID NO:5, paragraph 0089, and the promotor at position 222-245 in Fig.2) and the T7 promotor. Both promotors are located upstream of urease A and urease B is located downstream of the urease A gene. Both subunits are expressed together but due to the higher degradation of urease A, more urease B is present in the cell. PT7-97 is a derivative of pYZ97. The "cryptic" promotor is removed from pT7-97 and thus it only carries the T7 promotor. The citrate synthesis homolog corresponds to the frame HP 0026 (paragraph 0038). The sequences thereto are derived from Genbank. GroES, GroEL and HylB correspond to HP 0010, HP0011 and HP0599 (paragraphs 0036 and 0039). Thus the present invention has been applied to known proteins. In view of the cancellation of claims 1, 3, 5-11 and 13-23, the above discussion and the addition of new claims to the application,

applicants request that this rejection be withdrawn.

Claims 1, 6-10, 13 and 19-22 were rejected under 35 USC §112, second paragraph, as indefinite. Claims 1, 6-10, 13 and 19-22 have been canceled and new claims added to the application which do not include the language found indefinite. In addition, applicants point out that page 5, lines 2-12, discuss using attenuated bacteria as a DNA delivery vehicle for a target cell and page 7 of the present application discusses phase variable expression. In view of this disclosure, applicants respectfully contend that the newly added claims are not indefinite.

Claims 1, 5, 10, 11, 13, and17-21 were rejected under 35 USC §102(b) as anticipated by Doidge in view of McKee. Applicants point out that Doidge in view of McKee does not disclose the use of a Helicobacter immunogen consisting of urease A and urease B simultaneously. In view of the cancellation of claims 1, 5, 10, 11, 13 and 17-21, and the addition of new claims to the application, applicants request that this rejection be withdrawn.

Claims 1, 5, 10-11, 13-15, 17-22 and 23 were rejected under 35 USC §102(b) as anticipated by Michetti. Claims 1, 13-15 and 19-22 were rejected under 35 USC §102(e) as anticipated by Michetti. As discussed above, Michetti does not indicate that the combination of recombinant urease A and urease B in live vaccines leads to better results than the subunits alone since the recombinant subunits were tested separately and the live vaccine data was not available. Michetti discloses that the protective effect of urease A compared to urease B is delayed (col. 25, line 66 and tables 5 and 6) and is worse than urease B (col 27, line 4). Michetti concludes that the individual subunits themselves can be used separately as vaccines and thus leads away from the presently claimed invention where both subunits are simultaneously expressed. Attached to this response is a reference, Ferrero et al. (Infection

and Immunity, 1994, 62:4981-4989) which compares the protective effect of native urease to the immunogenic effect of the individual subunits. Ferrero shows that protection is obtained only with UreB not UreA. Thus, at the time the present invention was made, the prior art lead away from the simultaneous use of both subunits. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 1, 3, 5, 7-11, 13-15, 17-22 and 23 were rejected under 35 USC §103(a) as unpatentable over Michetti in view of Russell. As discussed above, Michetti does not indicate that the combination of recombinant urease A and urease B in live vaccines leads to better results than the subunits alone since the recombinant subunits were tested separately. Russell does not cure this deficiency as Russell teaches the expression of cholera toxin A2/B as a fusion protein to induce a humoral response. Russell does not suggest or disclose a protective live oral vaccine consisting of an attenuated Salmonella carrier that expresses a Helicobacter immunogen consisting of both urease A and urease B. In view of the cancellation of claims 1, 3, 5, 7-11, 13-15, 17-22 and 23 and the addition of new claims to the application, applicants request that this rejection be withdrawn.

Claims 1, 3 and 7-11 were rejected under 35 USC §103(a) as unpatentable over Russell in view of Bukanov. As discussed above, Russell does not suggest or disclose a protective live oral vaccine consisting of an attenuated Salmonella carrier that expresses a Helicobacter immunogen consisting of both urease A and urease B. Russell discloses expressing a single antigen as a fusion protein together with a further fusion protein as a streptococcus protein but does not suggest the expression of two Helicobacter antigens. Bukanov does not cure this deficiency as Bukanov only provides a genetic analysis of a variety of Helicobacter genes. Bukanov does not suggest or disclose the use of a Helicobacter immunogen consisting of both

urease A and urease B in a live vaccine. Neither Russell or Bukanov individually or in combination suggest or disclose that the combination of two specific Helicobacter antigens will provide better protection than a single antigen. In view of the above discussion and the cancellation of claims 1, 3 and 7-11, applicants request that this rejection be withdrawn.

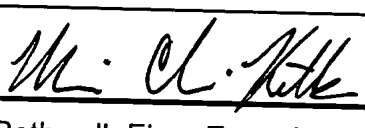
Claims 1, 5, 7-8, 10-11, 17-18 and 23 were rejected under 35 USC §102(e) as anticipated by Michetti. Claims 1, 13-15 and 19-22 were rejected under 35 USC §102(e) as anticipated by Michetti. As discussed above, Michetti does not indicate that the combination of recombinant urease A and urease B in live vaccines leads to better results than the subunits alone since the recombinant subunits were tested separately and the live vaccine data was not available. Michetti discloses that the protective effect of urease A compared to urease B is delayed (col. 25, line 66 and tables 5 and 6) and is worse than urease B (col 27, line 4). Michetti concludes that the individual subunits themselves can be used separately as vaccines and thus leads away from the presently claimed invention where both subunits are simultaneously expressed. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 1, 5 and 6 were rejected under the judicially created doctrine of obviousness type double patenting as unpatentable over claims 1, 5 and 6 of U.S. Patent No. 6,096,521 in view of Russell. Claims 1, 5 and 6 have been canceled and the newly added claims are not obvious over claims 1, 5 and 6 of U.S. Patent no.6,096,521 in view of Russell. In view of the cancellation of claims 1, 5 and 6, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 25 through 39 are now in condition for allowance. If it is believed that the application is not in condition for allowance,

it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

<table>
<tr><td colspan="6">RESPECTFULLY SUBMITTED,</td></tr>
<tr><td>NAME AND REG. NUMBER</td><td colspan="5">Monica Chin Kitts, Registration No.: 36,105</td></tr>
<tr><td>SIGNATURE</td><td colspan="2">  </td><td>DATE</td><td colspan="2">3/7/03</td></tr>
<tr><td>ADDRESS</td><td colspan="5">Rothwell, Figg, Ernst & Manbeck
Suite 800, 1425 K Street, N.W.</td></tr>
<tr><td>CITY</td><td>Washington</td><td>STATE</td><td>D.C.</td><td>ZIP CODE</td><td>20005</td></tr>
<tr><td>COUNTRY</td><td>U.S.A.</td><td>TELEPHONE</td><td>202-783-6040</td><td>FAX</td><td>202-783-6031</td></tr>
</table>

Enclosures: Ferrero article